Changes in the dielectric properties of rat tissue as a function of age at microwave frequencies

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Received 6 February 2001, in final form 26 March 2001

Abstract

The dielectric properties of ten rat tissues at six different ages were measured at 37 °C in the frequency range of 130 MHz to 10 GHz using an open-ended coaxial probe and a computer controlled network analyser. The results show a general decrease of the dielectric properties with age. The trend is more apparent for brain, skull and skin tissues and less noticeable for abdominal tissues. The variation in the dielectric properties with age is due to the changes in the water content and the organic composition of tissues. The percentage decrease in the dielectric properties of certain tissues in the 30 to 70 day old rats at cellular phone frequencies have been tabulated. These data provide an important input in the provision of rigorous dosimetry in lifetime-exposure animal experiments. The results provide some insight into possible differences in the assessment of exposure for children and adults.

1. Introduction

The dielectric properties of tissues have been widely studied, reviewed and reported (Schwan and Foster 1980, Pethig and Kell 1987, Gabriel *et al* 1996a, b). It is well established that the dielectric relaxation spectrum of a tissue extends over a wide frequency range extending from hertz to gigahertz, and that it consists of three main regions known as α , β and γ dispersions. The low-frequency α dispersion is associated with ionic diffusion processes at the site of the cellular membrane. The β dispersion extends over three to four frequency decades centred in the hundreds of kilohertz region, and is due mainly to the polarization of cellular membrane and organic macromolecules. Finally, the γ dispersion, in the gigahertz region, is due to the molecular polarization of tissue water (Gabriel 2000). The study of both α and β dispersions is outside the scope of this paper as the frequency range investigated extends from 130 MHz to 10 GHz, revealing the tail end of the β dispersion and a good part of the γ dispersion.

The water content of tissues varies throughout the lifetime of animals. For example, in mice the water content of the brain decreases from 85% when newly born to 77% for an

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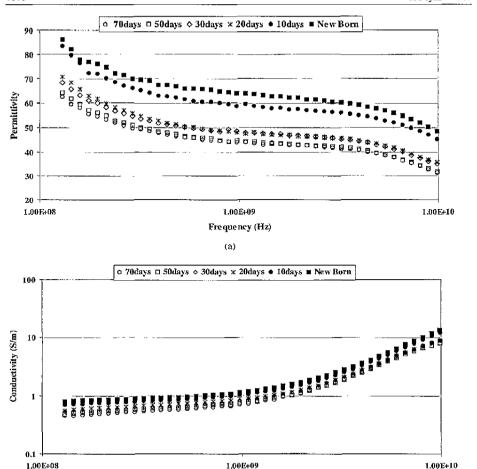


Figure 1. (a) Relative permittivity and (b) conductivity of *brain* tissue from rats of different ages in the frequency range of 130 MHz to 10 GHz.

adult (Uzman and Rumley 1958) such that one can anticipate corresponding variation in the dielectric properties at microwave frequencies.

Frequency (Hz)
(b)

The purpose of this work is twofold: first, to provide data for use in the assessment of exposure of animals to electromagnetic radiation at microwave frequencies, and second, to quantify the parameters of the γ dispersion and investigate their correlation with the water content of the tissue.

The extent of the variation of dielectric properties with age is particularly relevant to the rigorous assessment of exposure of experimental animals throughout their lifetime. It gives an indication into the extent to which variation in the dielectric properties need to be taken into consideration in the assessment of the exposure of children and adults as recently highlighted by the Independent Expert Group on Mobile Phones (IEGMP 2000).

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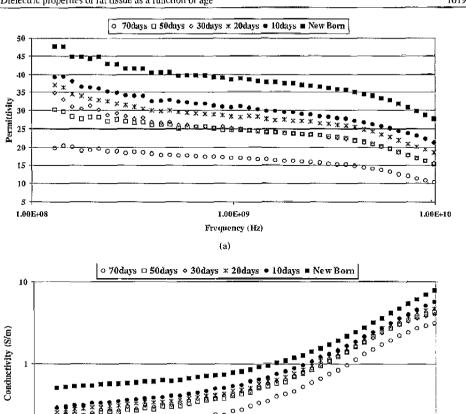


Figure 2. (a) Relative permittivity and (b) conductivity of *skull* tissue from rats of different ages in the frequency range of 130 MHz to 10 GHz.

While a strong variation of the dielectric properties of mouse and rabbit brain tissue has been observed with age (Thurai *et al* 1984, 1985), there are no equivalent data for other tissues. The data obtained in this study will add to those in the literature and provide data for rigorous dosimetry at microwave frequencies in lifetime animal studies and show that there are parallels between changes in the composition of tissues and the parameters of the γ dispersion.

1.00E+09

Frequency (Hz)

2. Material and methods

1.00E+08

Dielectric measurements have been carried out on brain, skin, skull, masseter muscle, salivary glands (submaxillary glands), liver, kidney, spleen, tongue and tail of Wistar strain rats, in the frequency range of 130 MHz to 10 GHz. The measurements were made using an open-ended coaxial probe and a computer controlled network analyser, following a previously reported

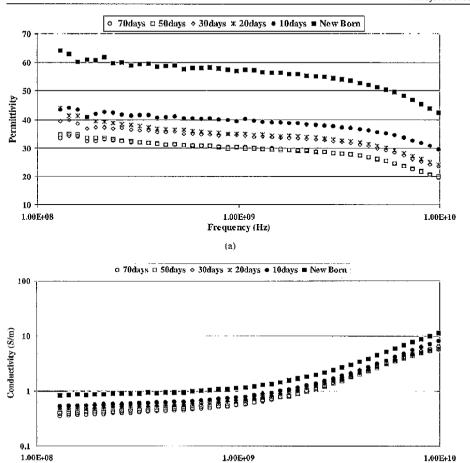


Figure 3. (a) Relative permittivity and (b) conductivity of *skin* tissue from rats of different ages in the frequency range of 130 MHz to 10 GHz.

procedure (Gabriel *et al* 1994). Small probes of 2.2 mm (inner radius = 0.256 mm and outer radius = 0.838 mm) and 3.5 mm (inner radius = 0.456 mm and outer radius = 1.49 mm) have been used in these experiments.

Frequency (Hz)
(b)

This procedure is suitable for dielectric measurement of biological tissue; its stated accuracy is between 1 and 2%, assessed by measurement on standard liquids of well known dielectric properties, and the reproducibility of a measurement is better than 1% (Gabriel *et al* 1994).

We have considered the following age groups: new-born (less than 24 hours old), 10, 20, 30, 50, and 70 days old. The 70 day old rat is considered a mature animal. All measurements were performed within 2-4 hours of the sacrifice of the animal. Care was taken to avoid loss of moisture from the tissue and to reduce to a minimum the handling of the samples. Physiological changes that are known to occur as a function of time after death affect mostly

Table 1. Dielectric data of different rat tissues at 900 MHz.

Age				Salivary						
(days)	Brain	Muscle	Skull	gland	Skin	Spleen	Liver	Kidney	Tail	Tongue
Permitti	vity at ~9	00 MHz (8.	81 × 10 ⁸	Hz)						
0	64.6	68.2	39.0	8.16	57.6	56.0	53.4	59.9	50. 1	59.5
10	59.5	62.0	31.0	57.9	39.8	55.1	54.4	60.0	36.1	60.2
20	48.5	49.6	28.7	47.4	35.1	53.9	48.3	46.9	25.4	50.6
30	49.2	51.2	25.6	47.1	35.0	52.6	46.6	48.3	23.6	47.0
50	44.3	48.8	24.7	44.9	30.0	50.2	45.9	45.9	20.2	50.5
70	44.3	49.1	17.3	45.3	30.4	48.5	45.8	43.8	17. 1	53.0
Conduct	ivity at ~	900 MHz								
0	1.1	1.3	0.8	1.3	1.1	1.2	1.0	1.2	0.9	1.2
10	1.0	1.2	0.5	1.1	0.8	1.2	1.0	1.2	0.6	1.1
20	0.8	1.0	0.4	0.9	0.7	1.1	0.9	1.0	0.4	0.9
30	8.0	1.0	0.4	0.9	0.7	1.1	0.8	0.9	0.3	0.9
50	0.7	0.9	0.4	8.0	0.6	1.0	8.0	0.9	0.3	0.9
70	0.7	0.9	0.2	8.0	0.5	0.9	0.8	0.9	0.3	1.0

Table 2. Dielectric data of different rat tissues at 1800 MHz.

Age (days)	Brain	Muscle	Skull	Salivary gland	Skin	Spleen	Liver	Kidney	Tail	Tongue
Permitti	vity at ∼l	800 MHz (1.78 × 10	^y Hz)						.,,
0	62.3	66.3	37.5	59.7	56.0	53.7	50.9	57.4	47.7	57.3
10	57.3	59.8	29.5	56.1	38.7	53.0	51.9	57.4	33,8	57.8
20	46.9	47.6	27.5	45.6	34.3	52.4	47.4	45.5	24.1	49.8
30	46.7	48.1	23.8	44.7	33.5	49.7	44.5	45.8	22.1	44.8
50	43.2	47.4	24.0	43.5	29.3	48.2	44.4	44.3	19.2	49.4
70	42.6	46.7	16.2	43.2	29.4	46.0	43.9	41.7	15.8	51.2
Conduct	tivity at ~	1800 MHz								
0	1.60	1.89	1.09	1.76	1.55	1.67	1.53	1.74	1.36	1.80
10	1.44	1.70	0.82	1.58	1.08	1.68	1.47	1.69	0.87	1.67
20	1.16	1.41	0.70	1.28	0.95	1.57	1.27	1.37	0.60	1.33
30	1.15	1.43	0.65	1.22	0.94	1.46	1.17	1.28	0.55	1.29
50	1.04	1.38	0.61	1.22	0.82	1.43	1.22	1.26	0.46	1.35
70	1.04	1.39	0.43	1.25	0.84	1.39	1.24	1.27	0.52	1.46

the dielectric data at low frequencies, the site of the α dispersion (Kraszewski *et al* 1982). At microwave frequencies the data are sensitive to the moisture content and much less affected the physiological processes that take place within hours of death. No preservative material has been used. Tissues were kept in small containers and placed in a water bath to maintain a 37 °C temperature. The sample thickness was at least four to five times the probe diameter to constitute a semi-infinite lossy sampling volume (Gabriel 1993).

At least five sets of measurements were made on each tissue and averages and standard deviations have been calculated. Skin has been measured from the inside rather than the outside in order to avoid contact with the covering fur. Tissues from new-born rat are in some cases too thin to provide sufficient sample volume: in such cases several tissue layers were used and care has taken to have a good contact with the probe prior to measurement. Measurements

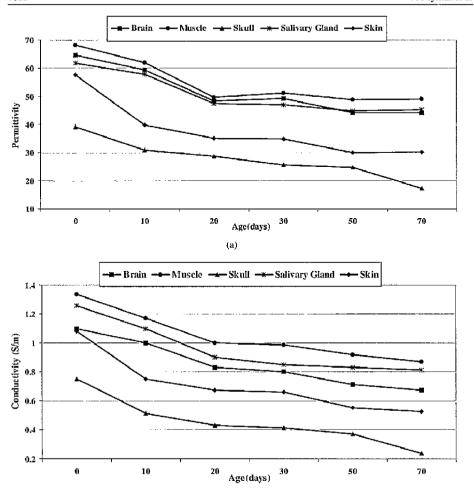


Figure 4. (a) Permittivity and (b) conductivity of rat tissue as a function of age at 900 MHz.

were repeated for three different rats at each age for brain, muscle, skull, skin, salivary glands and tongue. For the rest of the tissues two rats were measured at each age.

To quantify the γ dispersion, the data were fitted to the well known Cole–Cole expression:

$$\hat{\varepsilon}(\omega) = \varepsilon_{\infty} + \frac{\Delta \varepsilon}{1 + (j\omega \tau)^{(1-\alpha)}} + \frac{\sigma_i}{j\omega \varepsilon_0}$$

where $\hat{\varepsilon}$ is the complex relative permittivity and ω the angular frequency. $\Delta \varepsilon$, the amplitude of the dispersion, is defined as $\Delta \varepsilon = \varepsilon_s - \varepsilon_\infty$, where ε_∞ is the permittivity at high frequencies where $\omega \tau \gg 1$ and ε_s is the permittivity at low frequencies where $\omega \tau \ll 1$. τ is the relaxation time constant, and ω is a parameter that allows for the broadening of the dispersion. Finally, σ_i is an ionic conductivity term and ε_0 is the permittivity of free space. This is essentially an empirical formulation, not recommended for detailed mechanistic investigations. It is, however, quite suitable for comparative studies where there is a known, dominant interaction

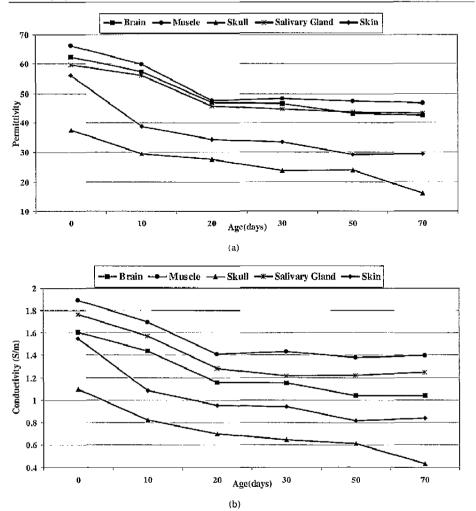


Figure 5. (a) Permittivity and (b) conductivity of rat tissue as a function of age at 1800 MHz.

mechanism such as the molecular rotation of tissue water as in this case (Gabriel et al 1996c).

The fitted parameters also allow some parallels to be drawn with the changes in tissue composition and in particular the water content. The analysis was carried out using a complex curve-fitting program. The data of each tissue at each age were fitted separately and the value for ε_{∞} was fixed at three. The choice of parameter value for ε_{∞} is based on the knowledge that the corresponding value for water is about five and that the water content of tissue is of the order of 60%. Moreover, a variation of about 20% on the value of ε_{∞} has very little effect on the other fitted parameters.

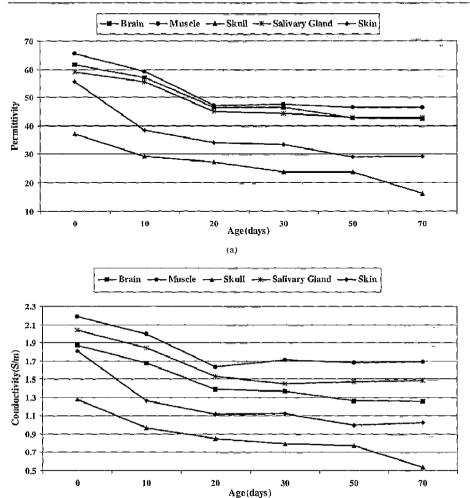


Figure 6. (a) Permittivity and (b) conductivity of rat tissue as a function of age at 2 GHz.

3. Results

The measured permittivity and conductivity data for brain, skull and skin are given in figures 1–3. Each data point is the average of multiple measurement on tissues from two or three rats. The standard deviations were calculated but omitted from the graphs for the purpose of clarity. The measurement errors discussed in the previous section contribute only a small part to the total uncertainty in the measurement of a biological tissue, where most of the uncertainty is due to inherent natural variability of the biological samples.

The variability in the measured values of permittivity of tissues from three rats in the frequency range of \sim 900–1800 MHz, ranged from about \pm 0.01 to 5%, depending on the tissue; the corresponding variability in conductivity ranged from \pm 0.1 to 8%.

Table 3. Changes in dielectric data of different tissues from 30 to 70 days in rat.

	% decrease i	n permittivity	% decrease in conductivity			
	900 MHz	1800 MHz	900 MHz	1800 MHz		
Brain	9,9	8.6	16.3	9.8		
Skall	32.5	31.9	42.5	32.9		
Skin	13.2	12.4	20.5	10.7		

Table 4. Variability (% standard deviation) in the dielectric measurements of 30 day old rat tissues at 900 and 1800 MHz.

	Permittivity (900 MHz)	Permittivity (1800 MHz)	Conductivity (900 MHz)	Conductivity (1800 MHz)
Brain	0.17	0.02	4.80	2.67
Skull	1.60	1.33	7.67	4.47
Skin	0.67	0.63	0.85	0.66

Table 5. Variability (% standard deviation) in the dielectric measurements of 70 day old rat tissues at 900 and 1800 MHz.

	Permittivity (900 MHz)	Permittivity (1800 MHz)	Conductivity (900 MHz)	Conductivity (1800 MHz)
Brain	1.08	1.08	6.15	5.56
Skull	4.28	4.33	5.16	6.87
Skin	1.89	1.31	7.9	5.8

Observed differences as a function of age are deemed significant if in excess of these innate variabilities.

Data for all measured tissues are reported in tables 1 and 2 and figures 4–6 at the GSM frequencies of 900 and 1800 MHz and at 2 GHz, a mid-frequency of the third generation universal mobile telecommunication system (UMTS).

The data show a general trend of decreasing permittivity and conductivity with increasing age for most of the tissues, the trend being generally in line with the decrease in the water content of the tissue as the animal ages. For brain, skull, skin salivary glands, muscle and kidney tissue the largest variations were observed between the ages of 0, 10 and 20 days. Smaller differences were observed for abdominal tissues between the ages of 30, 50 and 70 days compared to the corresponding values for brain, skin and skull tissue. The percentage decrease in the average permittivity and conductivity of these three tissues is given in table 3; the associated standard deviations expressed as percentage of the average are given in tables 4 and 5.

For each tissue the data above 600 MHz were fitted to the Cole-Cole expression; the fitted parameters and 95% confidence intervals for ten rat tissues at different ages are shown in table 6.

4. Discussion

The physiological development of an organism or tissue involves structural and biochemical changes; the rate at which the changes occur depends on the species and the type of tissue such that some tissues mature faster than other (Widdowson and Dickerson 1960). For example, foetal liver and kidney are much nearer to the biochemical composition of the adult organs than

Table 6. Dielectric parameters of water dispersion in tissues obtained by fitting the experimental results at $37\,^{\circ}$ C. The \pm term corresponds to the 95% confidence interval.

			τ_{relax}	$\pm au_{ m relax}$			σ	±σ
Tissue/age	$\varepsilon_{\rm s}$	$\pm \varepsilon_s$	(ps)	(ps)	α	$\pm \alpha$	(S m ⁻¹)	(S m ⁻¹)
Brain				-				
New born	65.0	0.3	8.23	0.30	0.11	0.01	0.140	0.002
10 days	60.0	0.3	8.06	0.29	0.10	0.01	0.130	0.002
20 days	49.4	0.4	7.83	0.46	0.18	0.02	0.110	0.003
30 days	49.7	0.4	8.31	0.47	0.18	0.02	0.098	0.003
50 days	45.8	0.5	8.38	0.56	0.19	0.02	0.091	0.003
70 days	44.8	0.3	9,40	0.38	0.12	0.01	0.086	0.002
Skull								
New born	39.9	0.2	9.21	0.31	0.17	0.01	0.097	0.001
10 days	32.5	0.3	10.05	0.43	0.24	0.01	0.06	0.001
20 days	30.2	0.5	11.04	1.03	0.25	0.03	0.05	0.003
30 days	27.1	0.6	12.72	1.49	0.28	0.03	0.042	0.003
50 days	27.8	1.0	13.55	2.96	0.32	0.03	0.042	0.005
70 days	18.3	0.3	15.60	1.44	0.32	0.04	0.036	0.003
Skin	10.5	0.5	13.00	1.44	0.22	0.02	0.024	0.001
New born	58.68	0.23	8.22	0.22	0.15	0.009	0.143	0.000
	-		8.81	-				0.002
10 days	40.48	0.17		0.24	0.12	0.01	0.099	0.001
20 days	36.58	0.46	9.32	0.71	0.21	0.03	0.086	0.003
30 days	36.35	0.59	9.44	0.89	0.24	0.03	0.079	0.003
50 days	31.12	0.30	11.08	0.60	0.15	0.02	0.069	0.002
70 days	31.06	0.19	12.27	0.42	0.11	0.01	0.066	0.001
Muscle								
New born	18.86	0.24	8.41	0.20	0.10	0.009	0.182	0.002
10 days	62.63	0.33	9.00	0.31	0.10	0.01	0.154	0.003
20 days	50.70	0.27	8.64	0.28	0.18	0.01	0.136	0.002
30 days	52.33	0.39	10.00	0.41	0.21	0.01	0.119	0.002
50 days	50.24	0.35	10.51	0.42	0.14	0.01	0.12	0.002
70 days	49.64	0.33	12.21	0.41	0.10	0.01	0.109	0.002
Salivary gland	ls							
New born	62.71	0.25	8.29	0.22	0.14	0.01	0.17	0.002
10 days	58.56	0.30	8.65	0.30	0.10	0.01	0.15	0.002
20 days	47.92	0.28	8.85	0.32	0.15	0.01	0.12	0.002
30 days	47.79	0.27	8.78	0.30	0.19	0.01	0.106	0.002
50 daγs	46.43	0.38	9.37	0.46	0.18	0.02	0.109	0.002
70 days	46.33	0.37	10.51	0.47	0.16	0.02	0.102	0.002
Liver								
New born	53.42	0.33	9.87	0.32	0.12	0.01	0.137	0.003
10 days	54.51	0.38	8.74	0.35	0.12	0.02	0.136	0.004
20 days	49.05	0.34	9.69	0.35	0.12	0.02	0.11	0.003
30 days	47.10	0.41	9.14	0.42	0.17	0.02	0.009	0.004
50 days	47.09	0.43	9.93	0.46	0.15	0.02	0.102	0.004
70 days	47.11	0.87	9.64	0.88	0.19	0.04	0.101	0.007
Spleen		2.01	,101	5.50		9.9.	J.1.J.1	0.007
New born	56.93	0.33	9.00	0.33	0.15	0.01	0.157	0.002
10 days	55.67	0.39	8.81	0.33	0.11	0.01	0.157	0.002
-								
20 days	54.63	0.34	9.09	0.36	0.13	0.01	0.150	0.003
30 days	53.65	0.29	8.05	0.28	0.23	10.0	0.133	0.002
50 days	51.71	0.38	9.40	0.41	0.17	0.02	0.130	0.003
70 days	50.25	0.57	9.54	0.62	0.23	0.02	0.118	0.003

Table 0. (Condition)		Table	6.	(Continued)	
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Tissue/age	$\mathcal{E}_{\mathcal{S}}$	$\pm \varepsilon_{s}$	τ _{relax} (ps)	±τ _{relax} (ps)	α	$\pm \alpha$	σ (S m ⁻¹)	±σ (S m ⁻¹)
Tongue	-							
New born	60.32	0.34	9.57	0.33	0.12	0.01	0.168	0.003
10 days	61.14	0.38	9.68	0.35	0.12	0.01	0.150	0.003
20 days	51.37	0.27	9.66	0.30	0.01	0.01	0.124	0.002
30 days	47.37	0.24	9.00	0.29	0.15	0.01	0.120	0.002
50 days	51.59	0.26	9.41	0.30	0.19	0.01	0.125	0.002
70 days	53.94	0.38	10.09	0.41	0.13	0.02	0.126	0.003
Kidney								
New born	60.09	0.30	8.98	0.24	0.13	0.01	0.160	0.003
10 days	60.05	0.45	8.35	0.38	0.11	0.02	0.165	0.004
20 days	47.37	0.39	9.80	0.41	0.12	0.02	0.128	0.004
30 days	48.60	0.42	8,52	0.41	0.18	0.02	0.117	0.004
50 days	46.76	0.43	9.61	0.46	0.14	0.02	0.112	0.004
70 days	44.80	0.74	10.28	18.0	81.0	0.03	0.107	0.006
Tail								
New born	50.99	0.41	9.16	0.45	0.17	0.02	0.115	0.003
10 days	36.90	0.45	8.95	0.68	0.20	0.03	0.070	0.003
20 days	26.52	0.43	11.49	1.01	0.22	0.03	0.039	0.003
30 days	24.60	0.36	11.08	0.93	0.26	0.03	0.036	0.002
50 days	21.50	0.39	11.29	1.17	0.28	0.03	0.028	0.002
70 days	18.32	0.27	16.99	1.38	0.25	0.02	0.033	0.001

are skeletal muscle or skin. As an animal matures, it goes through various stages of growth, which include changes in cells size, structure and the ratio of free to bound water. The data in table 6 show that for all tissues there is a decrease in the values of ε_s (and consequently the amplitude of the γ dispersion) as the animal grows older, which correlates with the reduction of the water content. For most tissues, there is a tendency of an increase in the value of τ and α with age that can be attributed to the changes in the proportion of free and bound water content of the tissues. The relaxation times are higher than 6.36 ps, the corresponding value for water.

The study of skin growth in human and pig by Widdowson and Dickerson (1960) reports changes in the ratio of free to bound water due to an increase in bound and a decrease in free water as the species grow from foetus to adult. This correlates with the systematic lengthening of the relaxation time (table 6).

In the case of brain, the brain tissue of the new-born, which consists predominantly of grey matter, undergoes numerous branching of dendrites during growth to form a more complex and highly structured tissue with a gradual change in the ratio of the grey and white matters. Grey matter is known to contain a higher proportion of water than white matter (Stewart-Wallace 1939). The variation in the dielectric properties of brain tissue is consistent with the previous research (Thurai *et al* 1984, 1985). It is also in line with the studies on the water content of rat brain, which is reported to fall rapidly with age from 9 to 45 days after birth (Donaldson and Hatai 1931). Figure 7 shows the comparison between the permittivity of mouse brain at different ages reported by Thurai *et al* (1984) and that of the rat observed in this study.

The skull hardens as it develops and increases its calcium content; it contains red bone marrow in young animals. The cellular composition of bone marrow varies in different regions of the skeleton. It also varies with the age of the individual. Nearly all the bones of the foetus contain red marrow; the colour indicates that the marrow is capable of producing blood cells. Following birth, the number of active haemocytoblasts (primitive stem cells that blood cells

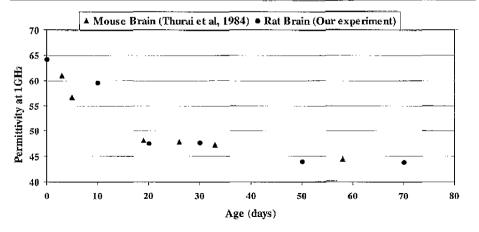


Figure 7. The permittivity of mouse brain at 1 GHz for different ages (Thurai *et al* 1984) compared with the permittivity of rat brain at different ages (our experiment).

are derived from) decreases in most areas of bone marrow, and they are replaced with fat cells (Spence 1990). The abundance of fat cells causes the colour of the marrow to change from red to yellow. In the adult most bones contain yellow marrow, with red marrow present only in the ends of certain long bones, the ribs, sternum, vertebrae and pelvis. The red marrow has higher water content compare to yellow bone marrow that is mostly found in adult long bones. These developmental changes have implications for the dielectric properties. The largest variations in dielectric parameters are those observed for skull and for the bony tail (table 6). For both tissues the decrease in permittivity and conductivity and the increase in relaxation time are the highest observed.

5. Conclusion

Among head tissue, brain, skin and skull exhibit the largest decrease in the permittivity and conductivity, as the animal gets older, while the corresponding changes for the abdominal tissues are less prominent. Skull has the highest percentage decrease in the conductivity (42.45%) at 900 MHz when the animal ages from 30 to 70 days old. This value is well above the variability in the measurement of the conductivity of the skull at the same frequency (7.67%). The results of the fitting procedure show that the Cole–Cole expression is a good description of the dielectric behaviour of tissue water.

The dielectric properties of each at microwave frequencies can be calculated from the parameters in table 6 and used for the provision of dosimetry in lifetime exposure animal experiments. It is also interesting to anticipate what the projection of these results would mean for the assessment of the exposure of children compared to adults.

Acknowledgments

This work was supported by the UK EPSRC studentship and a CASE award from Microwave Consultants Ltd to A Peyman.

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